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EXAMINER

LAMBERTSON, DAVID A

ART UNIT PAPER NUMBER

1636

DATE MAILED: 09/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

09/869,831

Applicant(s)

MATSUNAGA ET AL.

Examiner

David A. Lambertson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 July 2004.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) 7 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION***Election/Restrictions***

Applicant's election with traverse of Group I (claims 1-6 and 8) in the reply filed on July 1, 2004 is acknowledged. The traversal is on the ground(s) that the Examiner has incorrectly applied the standards for establishing Lack of Unity in the instant case. Applicant rationalizes that there are many "common technical features" that link the inventions of Groups I-II (see for example page 3, second paragraph), and that although the Examiner identifies a distinct technical feature between the groups of claims, this improperly ignores the "common features" of the invention (see for example page 3, second paragraph). This is not found persuasive because the proper manner for establishing a Lack of Unity involves an analysis of the "special technical feature," and not the "common technical feature" as alleged. As acknowledged by Applicant, "The Examiner's position identifies a distinct technical feature between the groups of claims;" as set forth in the original election/restriction requirement, this represents the "special technical feature" (i.e., the different method steps required to identify an agonist versus an antagonist) of the inventions, and properly breaks unity between the inventions. Furthermore, as indicated below, the "common features" noted by Applicant are themselves subject to prior art rejections, thus they cannot suffice as a "special technical feature" that defines the instant invention over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-8 are pending in the instant application. Claim 7 is withdrawn from consideration as being drawn to a non-elected invention. Claims 1-6 and 8 are under examination in the instant application.

Priority

Acknowledgment is made of Applicant's claim for foreign priority under 35

U.S.C. 119(a)-(d). The certified copy has been filed in the instant Application.

It is noted that the foreign priority document is in the Japanese language. Given the lack of a translation of the foreign priority document, the Office cannot adequately determine the level of priority between the instant claims and the priority document. As such, intervening references between the filing dates of the International Application and the foreign priority document will be applied as prior art.

Information Disclosure Statement

The information disclosure statements filed July 26, 2002 and July 6, 2001 have been considered, and a signed and initialed copy of the form PTO-1449s have been attached to this Office Action.

Specification

The disclosure is objected to because of the following informalities: the top of the first page of the claims states "Claims;" however, the claims must read in sentence format. It would be remedial to amend the first line of the Claims to read, "What is claimed is:" or "We claim:" in order to place the claims in the proper grammatical format.

Additionally, this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and

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(a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Specifically, page 11, lines 17-18 contain(s) a nucleotide sequence that is not identified by a SEQ ID NO, and which does not appear to be listed in the sequence listing. Applicant is required to provide a new sequence listing, both the paper copy and computer readable format (CRF), including all sequences encompassed by the definitions set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). In addition, applicant must provide a statement indicating the paper copy and CRF are the same, and that they do not incorporate new matter into the instant specification. Finally, applicant is required to amend the specification to clearly identify the sequence with its appropriate SEQ ID NO. In this instance, the nature of the non-compliance with 37 C.F.R. 1.821-1.825 does not preclude the examination of the application on the merits, the results of which are communicated below. However, failure to comply with all of the requirements of 37 C.F.R. 1.821-1.825 in response to this Office Action will be considered non-responsive.

Appropriate correction is required.

Claim Objections

Claim 5 is objected to because of the following informalities: claim 5 refers to non-elected subject matter; specifically, claim 5 refers to a method of identifying an antagonist.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

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Claim 5 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6 and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 and 8 are rejected for the use of the term "introduced to the chromosome." Specifically, it is unclear if this term means that the genes are covalently integrated into the chromosome of the cell, or if the genes need only be present in the same location as the chromosome (i.e., if the genes need only be in the nucleus at the same time as the chromosome). It is further unclear if both genes (a) and (b) must be introduced to the chromosome, or if only gene (b) must be introduced to the chromosome.

Claims 1-6 and 8 are rejected for the phrase "a promoter making no change of transcriptional activity from a ligand contact with the ligand responsive transcriptional regulatory factor." This phrase is not in the proper English vernacular, thus it is difficult to understand what

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the limitation is meant to encompass. For instance, it is unclear if the limitation is meant to indicate that transcription from the promoter is not affected by the ligand transcription regulatory factor that recognizes the upstream sequence of the first reporter gene, or if it is not affected by ligand responsive transcriptional regulatory factors in general.

Claim 5 provides for the use of a cell, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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The following rejections are predicated on the interpretation that the phrase "introduced to the chromosome" is intended to mean that the constructs are integrated covalently into the chromosome of the cell, and are not simply present in the same organellar location as the chromosome (i.e., the nucleus). Additionally, the reporter gene (b) is interpreted as being any gene that can be detected (i.e., any gene), so long as the gene is not the first reporter and is not operatively linked the same recognition sequence as the first reporter gene. Finally, as it regards kit claims, it is asserted that the kits are merely embodiments defined by the components of the kit; therefore, a reference collectively teaching the components of the kit is believed to also teach the kit.

Claims 1-6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,650,283 (Bradfield, et al.; see entire document; henceforth '283) in view of US 5,846,711 (Moore; see entire document; henceforth '711).

'283 teaches cells expressing both the Ah receptor (a ligand responsive transcription regulatory factor) and ARNT, and the use of these cells in assays to detect transcriptional activities of the receptor (see for example column 23, lines 30-33 and lines 41-46). The detection assay involves measuring the activity of a reporter gene that is operatively linked to a recognition sequence (i.e., a transcriptional response element (henceforth TRE)) for the Ah receptor (see for example column 2, lines 56-62). Both the Ah receptor and the reporter gene operatively linked to the Ah TRE are maintained episomally on plasmids, wherein each plasmid contains a selectable marker (see for example FIG. 11). The selectable markers function as reporter genes because they can be easily detected (that being the broadest reasonable

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interpretation of the term “reporters”); furthermore, these selectable markers are distinct from the first reporter gene, are not operatively linked to a TRE for a ligand responsive element and are not transcriptionally responsive to the presence of a dioxin. As a result, the selectable markers meet the limitation of reporter gene (b).

‘283 does not specifically teach the integration of their reporter genes into the chromosome of the host cell.

Moore teaches that the episomal maintenance of reporter genes and the integration of reporter genes into the host cell of a chromosome are interchangeable means for supplying a reporter to a host cell (see for example column 4, lines 9-15). It is well known in the art that the integration of reporters into the chromosome provides the added advantage of stability of copy number.

It would have been obvious for the skilled artisan to integrate the constructs taught by ‘283 into the host cell chromosomes because Moore teaches that the episomal maintenance of reporters is interchangeable with their integration into the chromosome. It would have been obvious to combine the teachings of Moore and ‘283 because the combined teachings both concern the ability to detect reporter genes, thus the teachings are functionally related. The ordinary skilled artisan would have been motivated to integrate the reporters of ‘283 into a host cell chromosome for the well-known advantage of stabilizing the copy number of the reporter gene, giving the advantage of a more consistent assay. Absent evidence to the contrary, the ordinary skilled artisan would have had a reasonable expectation of success when integrating the constructs taught by ‘283 into a host cell chromosome, as taught by Moore.

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Claims 1-6 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,432,692 (Bradfield, et al.; see entire document; henceforth '692) in view of US 5,846,711 (Moore; see entire document; henceforth '711).

'692 teaches the same subject matter of '283, as indicated by the incorporation of the patent by reference (see for example column 7, lines 55-60). Additionally, '692 explicitly teaches a cellular assay system for detecting agonists of the Ah receptor (referred therein as AHR)(see for example column 2, lines 46-52). This cellular system consists of a cell that has been genetically modified to express the Ah receptor, ARNT and additional proteins involved in AHR signaling from a plasmid (see for example column 2, lines 53-57). The method of detection involves measuring the level of expression of a reporter gene that is operatively linked to a dioxin responsive element, which is a ligand responsive TRE that specifically responds to activation of AHR (see for example column 2, lines 57-60). Considering the incorporation by reference of '283, '692 also teaches that these plasmids will have selectable markers. The selectable markers also function as reporter genes because they can be easily detected (that being the broadest reasonable interpretation of the term reporters); furthermore, these selectable markers are distinct from the first reporter gene, are not operatively linked to a TRE for a ligand responsive element and are not transcriptionally responsive to the presence of a dioxin. As a result, the selectable markers meet the limitation of reporter gene (b).

'692 does not specifically teach the integration of their reporter genes into the chromosome of the host cell.

Moore teaches that the episomal maintenance of reporter genes and the integration of reporter genes into the host cell of a chromosome are interchangeable means for supplying a

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reporter to a host cell (see for example column 4, lines 9-15). It is well known in the art that the integration of reporters into the chromosome provides the added advantage of stability of copy number.

It would have been obvious for the skilled artisan to integrate the constructs taught by '692 into the host cell chromosomes because Moore teaches that the episomal maintenance of reporters is interchangeable with their integration into the chromosome. It would have been obvious to combine the teachings of Moore and '283 because the combined teachings both concern the ability to detect reporter genes, thus the teachings are functionally related. The ordinary skilled artisan would have been motivated to integrate the reporters of '692 into a host cell chromosome for the well-known advantage of stabilizing the copy number of the reporter gene, giving the advantage of a more consistent assay. Absent evidence to the contrary, the ordinary skilled artisan would have had a reasonable expectation of success when integrating the constructs taught by '692 into a host cell chromosome, as taught by Moore.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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Claims 1-6 and 8 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 and 11-13 of copending Application No. 09/550,173 (henceforth '173). Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of '173 are species of the instant claims in their specifically preferred embodiments, and therefore make the instant claims obvious. Specifically, claims 1-9 of '173 concern animal cells (a specific embodiment of cells as recited in the instant claims) that have been modified to "securely maintain" two reporter genes, one being responsive to a ligand TRE (in some instances specifically responsive to AHR TRE and dioxin TRE [see claims 3 and 9]), and one being non-responsive to ligand TRE. As defined by the specification on page 12 of '173, "securely maintained" is exemplified as being a chromosomal insertion. As such, the ordinary skilled artisan would have reasonably defined "securely maintained" as being chromosomal integration based on the '173 specification. '173 further claims kits of these cells (e.g., claim 13) and methods of using the cells to detect agonist activity of a ligand receptor (e.g., claims 11-12). Because the claims of '173 are species claims that fall within the genus claims of the instant application, the '173 claims anticipate and therefore make obvious the claims of the instant application, thus they are subject to Obviousness Double Patenting statutes.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Allowable Subject Matter

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571) 272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David A. Lambertson, Ph.D.
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JAMES KETTER
PRIMARY EXAMINER